REMARKS

Status of the claims

Claims 1-61 are pending in the application. Claims 1-61 are rejected. Claims 38 and 40 are objected to.

Claims 1, 6, 37, 38, 40, 41, 43, 44, 45 and 56-61 are amended and claims 5, 42 and 55 are canceled herein. No new matter is added herein.

Claim Amendment

Claims 1 and 44 are amended to overcome the 35 U.S.C. §112, second paragraph rejection. These claims are amended by incorporating the limitations of canceled claims 5 and 42 in claim 1 and claim 55 in claim 44. Thus, amended claim 1 is drawn to a method for detecting drug resistance of HIV in a sample. Such a method comprises taking a culture of recombinant cells in which at least one of the recombinant cell comprises a reporter sequence comprising a promoter, an HIV-specific enhancer sequence and a reporter gene whose expression is regulated by binding of a HIV specific protein to the HIV-specific enhancer sequence, CD4, and one or more cell surface co-receptors for HIV. The cell surface co-receptors in such cells are each encoded by a heterologous sequence and expressed at an elevated level relative to the level of the corresponding cell surface co-receptor naturally expressed in a human cell such that productive infection of the recombinant cell by HIV is achieved. This productive infection of the recombinant cell is defined by HIV replication and the infection of non-virally-infected cells in the culture of the recombinant cells.

This cell culture is contacted with a first sample containing HIV or with a second sample containing reference HIV strain. This is followed by addition of an anti-HIV agent to the cell culture for the first sample and to the cell culture for the second sample. The level of expression of the reporter gene for the first sample and for the second sample is then determined, where no change or an increase in the expression of the reporter gene in the first sample compared to the expression of the reporter gene in the second sample indicates drug resistance of HIV in the sample. This amendment is supported by Example 3, Figs. 14, 16, 17A-17C, 18A, 18B of the instant invention.

Amended claim 44 is drawn to a method for detecting drug resistance of HIV in a sample. Such a method comprises taking a first cell culture containing CD4 and one or more cell surface co-receptors for HIV at sufficient levels such that productive infection by HIV is achieved. The first cell culture is contacted with a first sample containing HIV or with a second sample containing a reference HIV strain. An anti-HIV agent is then added to the first cell culture for the first sample and to the first culture for the second sample. This is followed by incubation of the first culture in the presence of the first sample and the anti-HIV agent and the first culture in the presence of second sample and the anti-HIV agent for a suitable period time.

Further, a second cell culture containing a reporter sequence comprising a promoter, an HIV-specific enhancer sequence and a reporter gene whose expression is regulated by binding of a protein specific to HIV to the HIV specific enhancer sequence, CD4 and one or more cell surface co-receptors for HIV at sufficient levels such that productive infection by HIV is achieved is taken. After incubation, the supernatent of the first cell culture for the first sample is transferred to the second cell culture. Similarly, the first culture for the second sample is transferred after incubation to the second cell culture. This is followed by determining the level of expression of the reporter gene in the second cell culture for the first sample and in the second cell culture for the second sample, where no change or an increase in the expression of the reporter gene in the second cell culture for the first sample compared to the expression of the reporter gene in the second cell culture for the second sample indicates drug resistance of HIV in the sample. These amendments are supported by Example 3, Figs. 15, 17D and 18C of the instant invention.

Additionally, claims 38 and 45 are amended by canceling "consisting of" which occurs twice. The word "tittering" in claim 40 is amended to "titering" is supported by the illustration in Fig. 13. Claim 18 is amended by replacing the phrase "capable of" with "effective in". Claim 41 is amended by reciting propagating in human blood cells. Either the dependency and/or claim language of claims 6, 37, 41, 43 and 45 are amended herein based on the amendments to their respective independent claims. Additionally, claims 52-58 are renumbered as claims 55-61respectively.

Claim objection

Claims 38 and 40 are objected to herein. Applicant respectfully traverses this rejection.

The Examiner states that claim 38 contains the phrase "consisting of" and claim 40 contains the word "tittering" which has a different meaning from what is intended.

Claims 38 and 40 are amended as discussed supra. The recitation of "consisting of" is canceled from the claim once. Additionally, Applicant submits that the word 'tittering" was misspelled and should have spelled "titering" instead (Fig. 13). Based on these amendments and remarks, Applicant respectfully requests the withdrawal of objection of claims 38 and 40.

Double Patenting rejection

Claims 1, 2, 8-12, 15, 18, 33 and 34 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 61-66 of U.S. Patent No. **6,900,010 B2**.

Claims 1-18, 24, 33, 34, 37 and 39 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 5, 9-24 and 26-28 of U.S. Patent No. **6,884,576 B2**. Applicant respectfully traverses this rejection.

The Examiner states that although the conflicting claims are not identical, they are not patentably distinct from each other because the limitations in the patented claims appear to be the same as in the instant claims. Based on this, the instant claims are anticipated by the patented claims.

Claims 1 and 44 and their dependent claims are amended as discussed supra and recite comparing the expression level of reporter gene in a sample containing HIV and a sample containing reference HIV strain. Hence, the recitation of these claims is not the same as the claims of the above-mentioned patents. Accordingly, Applicant submits that the instant claims are patentably distinct from those issued in the patents. Accordingly, based on this remark, Applicants request the withdrawal of rejection of claims 1, 2, 8-12, 15, 18, 33 and 34 over claims 61-66 of U.S. Patent No. **6,900,010 B2** and claims 1-18, 24, 33, 34, 37 and 39 over claims 1, 4, 5, 9-24 and 26-28 of U.S. Patent No. **6,884,576 B2**.

35 U.S.C. §112 Second Paragraph rejection

Claims 1-61 are rejected under 35 U.S.C. §112, second paragraph for being indefinite. Applicants respectfully traverse this rejection.

The Examiner states that claims 1 and 44 lack clarity for the following reasons. First, the claim language does not point the salient characteristics of the expression constructs inside the recombinant cells. Second, the definition of "productive infection" in claim 1 is confusing. Third, the recitation of "first sample" in claim 1 is incorrect since it lacks second or third sample. Fourth claims 1, 41 and 44 lack essential steps and elements such as a "wherein" clause. Fifth, claim 41 is missing the essential element and conditions for propagation of sample HIV. Sixth, claims 2-43 and 45-61 depend from indefinite claims. Seventh, claims 56 and 58-60 are renumbered and lack antecedent basis. Eighth, the phrase "capable of" in claim 18 renders the claim indefinite.

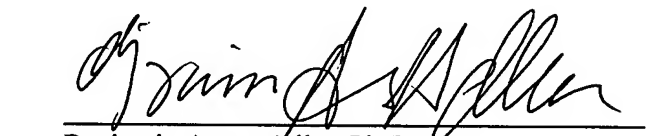
An inventive concept of the instant invention is generation of recombinant cell lines that overexpress CD4 and one or more co-receptors for HIV such as CXCR4 and CCR5 at high levels to render the cells susceptible to productive infection of various strains, subtypes or clades of HIV from both laboratory and clinical isolates and their use in detecting drug resistance of HIV in a sample. The anti-HIV agents comprise of inhibitors in the early stage and in the late stage of the viral replication. For instance, the early stage inhibitors may include but are not limited to entry inhibitors, reverse transcriptase inhibitors or integrase inhibitors while the late stage inhibitors may include but are not limited to protease inhibitors or virus maturation inhibitors (page 39, lines 17-25). The instant invention provides assays for detecting resistance to early stage inhibitors such as nucleotide and non-nucleotide RT inhibitors (claims 1-43; Figs. 14, 16, 17A-17C, 18A, 18B) and to late stage inhibitors such as protease inhibitors (claims 44-58; Figs. 15, 17D, 18C).

Such assays in general, comprise comparing the expression level of reporter gene in the culture contacted with HIV in a sample with the expression level of reporter gene in the culture contacted with reference HIV strain as indicated in the above-mentioned figures. Hence, claim 1 is amended to include the recitation of second sample. Additionally, claims 1 and 44 are also amended with regards to the recitation of salient characteristics of the expression constructs such as comprising promoter, HIV specific enhancer sequence and a reporter gene whose expression is regulated by binding of a HIV-specific protein and HIV specific enhancer sequence. Additionally, the definition of "productive infection" is amended as suggested by the Examiner.

Furthermore, claims 1 and 44 are amended to include the "wherein" clause. For instance, these claims include a determining level of expression of reporter gene in the culture in contact with HIV and the culture in contact with reference HIV strain, where no change or increase in the level of expression of the reporter gene in the cuture in contact with HIV compared to the culture in contact with HIV reference strain indicates that sample is resistant to the drug. Claim 41 is amended to recite that the HIV contained in the sample is propagated in human blood cells as illustrated in figure 13 of the instant invention. Additionally, claims 52-58 are renumbered. Furthermore, the recitation of "capable of" in claim 18 is replaced by "effective in". Hence, independent claims 1 and 44 and their dependent claims are no longer indefinite. Accordingly, based on the claim amendments and remarks, Applicant respectfully requests the withdrawal of rejection of claims 1-61 under 35 U.S.C. 112, second paragraph.

This is intended to be a complete response to the Office Action mailed March 22, 2007. Applicants enclose a Petition for Extension of time and Form PTO-2038 along with the response. Only in the absence of Form PTO-2038, please debit any applicable fees from Deposit Account No. 07-1185 upon which the undersigned attorney is allowed to draw. If any issues remain outstanding, please telephone the undersigned attorney of record for immediate resolution.

Respectfully submitted,



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